The Veterinary Record

FOUNDED BY WILLIAM HUNTING, F.R.C.V.S., 1888.

No. 30. JULY 26, 1941. VOL. 53.

PRELIMINARY TRIALS ON THE ADMINISTRATION OF SULPHONAMIDE E.O.S. AND OF 4:4'-DIAMINODIPHENYLSULPHONE TO NORMAL CATTLE AND TO CATTLE AFFECTED WITH STREPTOCOCCAL MASTITIS

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Sulphanilamide is being widely used in the treatment of *Str. agalactiae* mastitis in cattle. The value of this treatment is still a matter for assessment, but it may be accepted that some degree of success has attended its use. In some cases the udder may be sterilised but in other instances infection persists; nevertheless some clinical improvement is frequently reported. Unfortunately there is a substantial group of mastitis-infected cattle that shows little or no improvement after treatment with sulphanilamide, even when very large quantities of the compound have been given. Sulphanilamide therapy therefore is both hopeful and disappointing.

The present experiments were made in order to collect information on the therapeutic dose for cattle of sulphonamide E.O.S. and 4 : 4'-diaminodiphenylsulphone. When this information was obtained both compounds were used for the treatment of a few cases of *Str. agalactiae* mastitis in cattle. Both compounds were supplied by Imperial Chemical Industries, Ltd.

Sulphonamide E.O.S., the sodium salt of the N-*a* ethyl-sulphonic acid of sulphanilamide, NH_2SO_2–C$_6$H$_4$–NH·CH(CH$_3$)·SO$_3$Na is a white crystalline solid which, when dry, contains 53 per cent. of sulphanilamide. It is very deliquescent and it is highly soluble in water. Sulphonamide E.O.S. appears to be stable for some time in solution in water but tends to break down rather readily in acid solution setting free sulphanilamide. A similar breakdown probably occurs after it has been administered to animals, particularly when the acid region of the stomach is reached. If this is so, there appears to be no reason why it should differ from an equivalent amount of sulphanilamide in toxicity or in therapeutic effect. The results obtained with dairy cows described in the present investigation are in agreement with this supposition.

4 : 4'-diaminodiphenylsulphone, NH_2–C$_6$H$_4$–SO_2–C$_6$H$_4$–NH_2 is a pale buff-coloured powder which is not readily wetted by water and dissolves very slowly. Findlay (1937) gives its solubility as 0·01 per cent. in water at room temperature and slightly more in hot water; it is more soluble in dilute acid.

Long and Bliss (1939) say that 4 : 4'-diaminodiphenylsulphone is undoubtedly the most active chemotherapeutic agent that so far has been tested in experimental streptococcal infections in mice, but its acute toxicity is so great as to preclude its use in human clinical therapeutics. Findlay (1937) records that 4 : 4'-diaminodiphenylsulphone appears to be effective in staphylococcal infections.

In the experiments made to find a safe therapeutic dose of each of the compounds for cattle, normal heifers were used and the animals were all in milk when the present experiments started. None, however, was a heavily milking heifer as the animals had not been selected originally for their potential milk yields.

In some cases the same animals were dosed with both compounds, and in other instances two separate courses of treatment with the same compound were given to the same heifer. Whenever the animals received two treatments an adequate interval of rest between treatments was allowed so that the effects of the first treatment had passed off before the second treatment was started. No facilities for weighing the heifers were available, but from their appearance it was judged that all were approximately of the same weight which was estimated at 1,000 lb. each. With those given sulphonamide E.O.S. determinations were made on the sulphanilamide in the blood and milk, and when 4 : 4'-diaminodiphenylsulphone was administered determinations of this compound in the same body fluids were made.

The method of estimation used was essentially that described by Marshall and Litchfield (1938) in which the NH_2-group is diazotised and the diazo compound is coupled with dimethyl *a*-naphthylamine in acid solution and the resulting red azo-dye is estimated colorimetrically. A weaker solution of dimethyl *a*-naphthylamine was, however, used and excess nitrous acid was destroyed with urea as described by Proom instead of with ammonium sulphamate before coupling. The amount of red azo-dye formed is not directly proportional to the amount of free sulphanilamide or 4 : 4'-diaminodiphenylsulphone present, but results within the usual limits of accuracy of colorimetric measurements are obtained by using near standards for comparison. The method estimates both sulphanilamide and sulphonamide E.O.S., but the latter quantitatively only after it has been in contact with acid for a while. From the fact that higher values were not obtained when blood and milk samples were kept in contact with acid (see below) it seems that the amount (if any) of sulphonamide E.O.S. in them was exceedingly small.

Some difficulty was experienced in precipitating proteins, particularly milk proteins, completely, and it was found that several hours' contact with the precipitating acid was necessary to obtain a filtrate in which the dye could be developed satisfactorily. It might be expected that long contact with acid would tend to hydrolyse conjugated compounds of sulphanilamide or 4 : 4' diaminodiphenylsulphone but tests showed that this is not so. There is, in

fact, a slight reduction in the amount of free drug to a constant figure after 1 hour as shown by tests made after 5 minutes, 1 hour (the usual time), 4 hours and 22 hours' contact with acid before filtering. The cause of this is not known. A period of 18 hours (overnight standing) was used for convenience.

5 ml. of blood were collected from the jugular vein and immediately added to 75 ml. of distilled water and the diluted blood left for 30 minutes to complete haemolysis. To 20 ml. of diluted blood, 5 ml. of 20 per cent. *p*-toluene sulphonic acid were added to precipitate proteins and after standing overnight the mixture was filtered through a 9 cm. Whatman No. 2 filter paper. To 5 ml. of the filtrate in a test tube, 0·5 ml. of 0·1 per cent. $NaNO_2$ solution was added and after 1 minute excess nitrous acid was destroyed by adding 0·25 ml. of a saturated solution of urea. The mixture was shaken occasionally and after 10 minutes 2·5 ml. of $M.NaH_2PO_4$ solution and 5 ml. of 0·1 per cent. alcoholic dimethyl *a*-naphthylamine (V/V in 95 per cent. alcohol) were run in and mixed by inversion; 15 minutes were allowed for full colour development to be reached and the colour then compared in a Klett colorimeter with that of a near standard which had been prepared in a similar way.

The samples of milk that were examined were obtained from the pooled milk from all four quarters of the udder, each quarter being milked out on the occasions when samples were taken. 1 ml. of freshly drawn milk was diluted with 15 ml. of water and after 30 minutes 4 ml. of 20 per cent. *p*-toluene sulphonic acid were added to precipitate proteins. The subsequent procedure was the same as for blood.

Standard solutions of sulphanilamide and 4 : 4′-diaminodiphenylsulphone were prepared in 4 per cent. *p*-toluene sulphonic acid from stock solutions containing 20 mg. per cent. of sulphanilamide and 10 mg. per cent. of 4 : 4′-diaminodiphenylsulphone respectively in 4 per cent. *p*-toluene sulphonic acid. Standard solutions were renewed weekly and stock solutions monthly. Both stock and standard solutions were kept in a refrigerator when not in use. It was found that solutions of both drugs in pure water deteriorated slowly, presumably by biological action, even when kept in a refrigerator and much more rapidly at room temperature. Solutions in 4 per cent. *p*-toluene sulphonic acid were much more stable. 5 ml. of standard solution were treated in the same way as the blood and milk filtrates. Suitable standards of sulphanilamide contained 0·25, 0·5, 0·75, 1·0, 1·25 and 1·5 mg. per cent., equivalent to 5, 10, 15, 20, 25 and 30 mg. per cent. in blood and milk. Suitable standards of 4 : 4′-diaminodiphenylsulphone contained half these quantities. Solution of 4 : 4′-diaminodiphenylsulphone may be aided by first wetting it with alcohol.

When repeated doses of either compound were given to the same animals these were administered daily at 6 a.m. and 6 p.m. and blood and milk samples were collected at 3 p.m. or nine hours after the morning treatment.

The Administration of Sulphonamide E.O.S. to Normal Cattle

As the above compound is very soluble in water, preliminary trials on its inoculation by the subcutaneous route were made in guinea-pigs, but the inoculation of 0·5 to 1 c.c. of a 50 per cent. solution was found to cause severe irritation and it produced extensive necrosis of the subcutaneous tissues. Because of these findings it was considered inadvisable to give subcutaneous inoculations to cattle.

Two heifers were given intravenous inoculations; one received 45 grammes dissolved in 45 c.c. of distilled water and the other was given 90 grammes dissolved in 180 c.c. of distilled water. Eight hours after inoculation only small quantities of sulphanilamide were found in the blood and milk of the former animal and two hours later the amount in the blood had decreased and there was none in the milk. The animal given 90 grammes in the right jugular vein was bled from the opposite vein ten minutes later and 22 mgs. per cent. of sulphanilamide was present in the blood. Three hours later 70 per cent. of this had disappeared; six hours after inoculation 88 per cent. had been removed and by the twelfth hour only a trace of sulphanilamide was present in the blood. Some hours after inoculation sulphanilamide was found in the milk in rather smaller amounts than in the blood. These experiments showed that following the intravenous inoculation of sulphonamide E.O.S., sulphanilamide was rapidly eliminated from the blood and milk, which indicated that intravenous inoculation was not promising when the object was to maintain a relatively constant and high concentration of sulphanilamide in the blood for several hours. Further trials were therefore confined to the oral administration of sulphonamide E.O.S., the requisite dose being dissolved in from 500 to 1,000 c.c. of tap water and the animals drenched from a bottle.

From Table I it will be seen that following the oral administration of a single dose, the sulphanilamide content of the blood and milk remained at approximately a constant level from the sixth to the twelfth hour. When this is compared with the rapid disappearance of sulphanilamide from the blood after an intravenous inoculation of sulphonamide E.O.S. it is apparent that the absorption of the compound from the alimentary tract must be relatively prolonged. In view of this it was decided to give multiple doses at 12-hour intervals.

Table II shows that when a constant dose is given every 12 hours greater concentrations of sulphanilamide are obtained in both the blood and the milk than when a single dose is given. This cumulative effect reaches a peak by the second or third day and thereafter the sulphanilamide in both the blood and the milk is maintained throughout the course of treatment at a more or less constant level, although appreciable fluctuations do occur.

When the data in Table III (p. 432) are compared with those shown in Tables I and II it appears that an initial high dose followed by multiple smaller doses does not necessarily maintain the sulphanilamide content of the blood at a higher level than when the initial dose is omitted. Great variations are, however, shown by individual animals receiving similar doses; this is illustrated by the figures for heifer RB in Table II and for heifer LB in Table III, and it is obvious that no definite conclusions on the value of an initial high dose or the effect of its omission are warranted from the observations that were made.

In order to have a basis for a comparison of the sulphanilamide content of the blood and milk of cattle treated with sulphanilamide, two animals were given sulphanilamide by the mouth and blood and milk samples were examined for sulphanilamide. The results of these examinations are shown in Table IV (p. 432.)

The readings obtained on the blood and milk from the two cattle in Table IV are appreciably higher than those obtained from animals given comparable quantities of sulphanilamide *a*-ethyl sulphonate. If the therapeutic properties of this compound are dependent on the sulphanilamide that is dissociated from it and on the quantity of sulphanilamide that is

TABLE I

Determinations of Sulphanilamide in mgm. per cent. after a single dose of Sulphonamide E.O.S.

Heifer.	Amount.	Hours after treatment.									
		3		6		9		12		33	
	Grammes.	B	M	B	M	B	M	B	M	B	M
R.B.	45	2·4	0·6	2·9	1·3	2·3	1·0	1·8	0	0	0
33	90	3·5	2·5	5·2	1·9	5·6	2·8	6		Tr.	0
29	180	5·0	2·2	9·4		8·1	8·8	8·6	7·4	2·2	2·6
31	360	10·7	9·5	23·5	18·8	24·0	28·8	28·8	21·8	17·1	19·0

B = Blood ; M = Milk.

TABLE II

Determinations of Sulphanilamide in mgm. per cent. following the administration of a constant dose of Sulphonamide E.O.S. every 12 hours

Heifer.	Amount Grammes.	Period of reatment tin days.	Days after treatment began.																									
			2nd		3rd		4th		5th		6th		7th		8th		9th		10th		11th		12th		13th		14th		15th		16th	
			B	M	B	M	B	M	B	M	B	M	B	M	B	M	B	M	B	M	B	M	B	M	B	M	B	M	B	M	B	M
36	45	14	3·6	4·5	4·6	7·8	5·5	6·3	4·8	7·6	6·2	7·4	5·7	5·3	6·7	7·3	5·2	3·7	6·7	3·8	8·4	3·7	7·3	3·8	7·0	4·1	5·0	5·0	10·0	13·5	5·9	6
B.R.	90	5½	12·6	14·0	29·9	20·7	16·5	17·3	18·4	20·2	18·3	25·7	3·6	4·5																		

B = Blood ; M = Milk.

TABLE III

Determinations of Sulphanilamide in mgm. per cent. following the administration of a large dose of Sulphonamide E.O.S. succeeded by a smaller and constant dose every 12 hours.

Heifer.	Amount. Initial dose. Grammes.	Amount. Subsequent doses. Grammes.	Period of treatment in days.	Days after treatment began. 1st B	1st M	2nd B	2nd M	3rd B	3rd M	4th B	4th M	5th B	5th M	6th B	6th M	7th B	7th M	8th B	8th M	9th B	9th M	10th B	10th M	11th B	11th M
S.B.	180	90	7	10·0	9·4	12·4	10·9	9·7	7·1	16·6	12·9	15·4	11·0	14·3	10·5	19·8	14·3	12·6	9·9	1·7	2·8	Tr.	2·8	0	0
L.B.	360	90	3½	10·4	8·0	14·0	11·6	18·3	11·5	11·0	11·2	3·9	3·8	0·7	0·5	0	0								
32	360	180	3½	10·5	9·9	23·0	24·9	28·3	24·3	15·7	13·0	7·4	9·1	2·1	2·3	Tr.	Tr.	Tr.	0						

The treatment of heifer L.B. stopped after 3½ days, that is after the 7th dose had been given, the supply of sulphanilamide E.O.S. being temporarily exhausted. The treatment of 32 was stopped after 3½ days because of the toxic symptoms produced by the large quantities of the compound that had been given.

B = Blood; M = Milk.

TABLE IV

Determinations of Sulphanilamide in mgm. per cent. after a large dose of Sulphanilamide followed by a smaller dose every 12 hours.

Heifer.	Initial dose. Grammes.	Subsequent doses. Grammes.	Period of treatment in days.	Days after treatment began. 2nd B	2nd M	3rd B	3rd M	4th B	4th M	5th B	5th M	6th B	6th M	7th B	7th M	8th B	8th M	9th B	9th M
22	150	50	7	24·2	23·9	25·1	26·0	26·3	25·4	23·2	26·3	26·4	29·1	34·0	29·0	23·0	25·1	10·0	13·0
29	180	90	7	29·8	34·8	34·8	36·5	41·6	45·6	43·0	41·6	40·2	49·6	58·4	50·0	59·0	59·8	33·6	36·2

B = Blood; M = Milk.

found in the blood stream, it is evident that sulphonamide E.O.S. will be of less value than sulphanilamide unless indeed larger doses of the former compound can be given without producing toxic symptoms.

The Toxicity of Sulphonamide E.O.S. for Cattle

All the cattle treated orally except the two that received single doses of 45 and 90 grammes respectively suffered from diarrhoea. A single dose of 90 grammes may, however, cause diarrhoea. Quantities of 180 to 360 grammes caused profuse watery diarrhoea within a few hours of the animals being drenched, and cattle that received repeated doses of 90 grammes or more suffered from diarrhoea throughout the period of treatment. Fluctuations were shown in the quantity and consistency of the faeces. Diarrhoea may be accompanied by intestinal irritation and during treatment two of the animals were observed to pass blood-stained mucilaginous material from the rectum. When the diarrhoea was profuse there was a noticeable falling off in the condition and with some animals the coat became rough and staring. The appetite during the period of treatment was sometimes impaired and concentrates were refused or only a portion of the usual ration was eaten. The severity of the symptoms was not necessarily relative to the size of the doses given. For example, one heifer (heifer BR, Table II) which received multiple doses of 90 grammes was much more seriously upset by the treatment than some that received the same or larger quantities of the compound. While diarrhoea or loss of appetite lasted, and for a few days afterwards, the milk yield was reduced. At the termination of treatment the animals quickly recovered their normal health, but condition was more slowly regained. Symptoms of nervous derangement were noticed in one animal, heifer 32, that received 360 grammes, followed every 12 hours by 180 grammes until 1,440 grammes had been given over a period of three and a half days.

On the morning of the fourth day when the final dose was given the heifer was dull; four hours later it was lying down and did not attempt to rise when approached. Its coat was staring; the skin of the forehead was furrowed by wrinkles; the eyes appeared sunken and the skin round the eyes, particularly over the orbital crests, was drawn into wrinkles; the left eye was occasionally partly closed as though it was painful; the facial expression was haggard; the pulse and temperature were normal but the ears were cold; coffee coloured fluid was passed involuntarily on occasion from the rectum. The animal rose with difficulty and balanced itself precariously on three legs while one foreleg was extended forward and lowered until the foot was about to touch the ground and then violently flexed. These movements of the foreleg were repeated until contact with the ground was made and the leg bore weight. The opposite foreleg was then extended and flexed in the same peculiar manner. Finally, the animal backed a few paces and stood with arched back and hind-quarters supported against the wall of the yard. A few hours later there was a great improvement in the condition and appearance, and the animal was able to walk a short distance though slowly. The next day, except possibly for slight swaying of the hindquarters when walking, nervous symptoms had disappeared and the expression was normal.

There was no evidence that treatment caused any abnormal fluctuations in the rectal temperature of the animals. The breath of all of the cattle during and for a short time after treatment had a characteristic smell which could be detected when standing behind those that had had the larger doses as they were tied up in the milking shed. The smell resembled that of cordite.

If sulphonamide E.O.S. were to be as valuable as or more valuable than sulphanilamide it would have to be shown that the former compound was the less toxic and that greater doses could be given with safety in order to raise the sulphanilamide content of the blood and of the milk to the same level as that which may be reached by giving a lesser dose of sulphanilamide. Experience in the administration of sulphanilamide to cattle in the field indicates that animals in different herds show great variations in their tolerance to the compound, and it is possible that these variations may be due to differences in the environment and the management of the animals. It therefore appears unsatisfactory to compare the toxicity of sulphanilamide as used in the field with the toxicity of sulphonamide E.O.S. when it was administered to the experimental animals. Two of the experimental animals were, however, given sulphanilamide and both were upset by the treatment to about the same degree as were those heifers that received comparable doses of sulphonamide E.O.S. The two animals receiving sulphanilamide, however, showed much higher concentrations of that compound in the blood and milk than did any of the heifers treated with sulphonamide E.O.S. It therefore appears unlikely that the sulphanilamide content of the blood and milk can be raised to a given level with greater safety by the administration of sulphonamide E.O.S. than by giving sulphanilamide.

The Administration of 4 : 4′-Diaminodiphenylsulphone to Normal Cattle

On account of the high toxicity of this drug for mice the initial doses given to cattle were small. The compound is relatively insoluble in water and its administration was therefore confined to the oral route, suspensions being shaken up in convenient quantities of water and administered in the usual way. The quantities given and the determination of 4 : 4′-diaminodiphenylsulphone in the blood and milk of normal cattle are recorded in Tables V and VI (*over-leaf*).

When single doses were given the highest concentration of 4 : 4′-diaminodiphenylsulphone in the blood was obtained at nine hours but subsequent readings were not in all cases progressively lower. For example, with animal No. 39 the reading at 28 hours was higher than at 12 hours and at 33 hours it was higher than at 28 hours. Those animals that received multiple doses, the initial dose being three to four times larger than subsequent doses, showed considerable daily fluctuations in the blood content of 4 : 4′-diaminodiphenylsulphone, but the concentration was generally well maintained over the period of treatment. From these observations it is concluded that the absorption of the compound was continued over a rather prolonged period, and that during this time there were occasions when its absorption into the blood stream was more rapid than its elimination from the blood stream. It would therefore appear that in the treatment of cattle suffering from *Str. agalactiae* or other infections, with 4 : 4′-diaminodiphenylsulphone, it would be rational to dose the animals at intervals of not less than 12 hours.

TABLE V.

Determinations of 4 : 4'-Diaminodiphenylsulphone in mgm. per cent. after a single dose of that compound.

Heifer.	Single dose.	Hours after treatment.																					
		4		6		9		12		28		33		38		51		58		81		105		130	
	Grammes.	B	M	B	M	B	M	B	M	B	M	B	M	B	M	B	M	B	M	B	M	B	M	B	M
32	72	5·3	1·0	3·8	0	8·6	1·3	3·3	0	0		1·8	0												
39	150	4·7	1·8	6·2	2·1	6·6	2·2	2·9	0	3·0	0	3·4	0	1·7	0	1·4	0	1·1	0	0·5	0	2·2	0	0	0

B = Blood ; M = Milk.

TABLE VI

Determinations of 4 : 4'-Diaminodiphenylsulphone in mgm. per cent. following the administration of a dose of that compound succeeded by a smaller and constant dose every 12 hours.

Heifer.	Initial dose.	Subsequent doses.	Period of treatment in days.	Days after treatment began.																			
				1st		2nd		3rd		4th		5th		6th		7th		8th		9th		10th		11th		12th	
	Grammes.	Grammes.		B	M	B	M	B	M	B	M	B	M	B	M	B	M	B	M	B	M	B	M	B	M
S.B.	18	4·5	7							2·8	0·7	2·7	0·6	2·9	0·4	1·8	0·5	0·2	0	0·3	0				
29	18	4·5	7							2·4	0·2	2·7	0·6	3·0	0·2	1·8	0·06	0·5	0	0·2	0				
22	36	9	7	2·4	0·6	1·9	0	3·2	0·6	1·6	0	4·6	Tr.	2·9	0	2·8	Tr.								
28	80	20	7			6·0	2·0	5·7	1·5	5·8	2·0	5·3	0·5	4·2	0·8	3·8	0·8	3·4	0·6	1·9	0·6	0·7	Tr.	Tr.	Tr.
L.B.	120	30 60	7 2½			7·1	3·2	6·5	1·9	7·5	1·4	5·6	1·0	3·5	0·5	3·5	0·7	3·1	0·5	5·6	4·2	6·0	5·5	4·5	5·5	1·2	2·4
22	120	40	7	16·5	7·4	14·7	7·2	18·5	8·8	12·1	4·4	13·2	4·8	14·7	4·75	16·2	4·7	6·6	1·9	2·6	1·2	1·9	Tr.		
28	180	90	1	12·6	5·8	13·1	10·2	7·7	5·8	3·4	2·7	2·6	1·6	1·9	0										

B = Blood ; M = Milk.

The Toxicity of 4 : 4′-Diaminodiphenylsulphone for Cattle

In mice the toxic symptoms are reported to be an aimless running about followed by paralysis that may last for two or more days. The only heifer that showed toxic symptoms related to nervous derangement was heifer 28 that received 180 grammes followed 12 hours later by 90 grammes.

Twenty-four hours after the first dose had been given the heifer was found lying down, and it was reported to have risen to its feet with great difficulty and to have had difficulty in walking. Four hours after this the animal was seen standing in a partly stupefied condition and showed twitchings of groups of body muscles; when forced to walk it moved slowly and its movements were ill-co-ordinated. A few hours later the symptoms had subsided and the animal appeared to be merely dull and lethargic. On the 2nd, 3rd, 4th, 5th and 6th days after treatment no concentrates were eaten and the milk yield dropped. The faeces were only slightly more liquid than normal during the 1st and 2nd days. Recovery from all symptoms was complete. The only other animal that showed any signs of being upset was No. 22. On the second and third days of treatment the heifer did not eat its concentrates and the milk yield dropped. These two animals, the only ones to show symptoms, received the largest doses. It is, however, interesting to note that cow No. 28, which received the larger dose and showed nervous symptoms, never had such a high concentration of 4 : 4′-diaminodiphenylsulphone in her blood as had animal No. 22.

From these observations it was concluded that cattle tolerate 4 : 4′-diaminodiphenylsulphone well.

The Treatment of Cows Suffering from *Str. agalactiae* Mastitis with Sulphonamide E.O.S.

Cow 445.—Infection was first detected in this animal in July, 1940. *Str. agalactiae* was again recovered from the left forequarter in October. Treatment commenced on November 22nd, 1940, and at this time clots were present in the fore milk from the left forequarter. An initial dose of 4 oz. was given and this was followed every 12 hours by 2 oz. and treatment was continued for 14 days. From the 4th day of treatment and until treatment stopped the milk from the affected quarter was normal in appearance. Clots were, however, again detected in the milk on December 8th and by December 24th the clots were large and the milk yellowish in colour. A bacteriological examination made on December 18th showed large numbers of *Str. agalactiae* in the milk from the affected quarter.

Cow 451.—Infection was first detected in May, 1940. *Str. agalactiae* was found in the milk from all four quarters in November, 1940. At this time the fore milk from both forequarters contained large clots: a few small clots were present in the fore milk from the right hindquarter. Treatment began on November 19th and was continued for 14 days. The doses of sulphonamide E.O.S. were similar to those given to cow No. 445. By the evening of the 2nd day of treatment only small clots were present in the fore milk and by the following day the milk was normal in appearance. This improvement lasted until a short time after treatment stopped, but by December 8th a small clot was found in the fore milk from the right forequarter. On centrifuging quarter milk samples collected on the last day of treatment only a small excess of sediment was obtained from the left fore and both hindquarters, but *Str. agalactiae* was isolated from these three quarters. The cow was turned out as dry soon after December 8th and no more observations were made.

Cow 481.—This cow was found infected in three quarters with *Str. agalactiae* in October, 1940. Before she received treatment clots were being passed in the fore milk from two of the affected quarters. Treatment commenced on December 3rd. An initial dose of 4 oz. was given, followed by 2 oz. every 12 hours for 14 days. During treatments and for a short time afterwards, the milk from the affected quarters retained a normal appearance, but by December 24th small clots were found in the fore milk from two quarters and a bacteriological examination made on January 3rd, 1941, showed *Str. agalactiae* in all three quarters originally affected. Some clinical improvement was, however, maintained for at least five weeks after treatment stopped.

Cow 541.—This animal was an old case of *Str. agalactiae* infection that suddenly assumed an acute character. Before treatment began the udder was tense and painful and the greatly diminished secretions drawn from it were greyish in colour and tinged with blood. The doses of sulphonamide E.O.S. were similar to those given to the other cows and treatment was continued for eight days, when it was stopped owing to the supply of the compound being exhausted. Sulphanilamide was then administered for another period of six days. The cow was not seen until a few days after the latter course of treatment had been completed and by this time there was a great improvement in her general condition and in the state of the udder, although that organ was still swollen and the secretions were unfit for consumption. The owner, however, reported that improvement was noticed three days after the treatment with sulphonamide E.O.S. started and that the udder secretions assumed an appearance more akin to that of normal milk.

All the cows treated suffered from diarrhoea during treatment and the owner complained that the treatment affected the cows adversely and in one case in particular caused a temporary drop in the milk yield.

The treatment had a beneficial effect in so far as it temporarily masked the grosser physical abnormalities of mastitis milk, and while treatment lasted and for a short time afterwards clots were not found in the milk of the two more chronic cases. The treatment of an acute case relieved the severity of the symptoms and in so far it was valuable. There was, however, in no case evidence of cure, as *Str. agalactiae* continued to be excreted in as large numbers after treatment as before treatment.

The Treatment of Cows Suffering from *Str. agalactiae* Mastitis with 4 : 4′-Diaminodiphenylsulphone

Cow 641.—Quarter samples from this cow were tested on December 1st, 1940, and large numbers of *Str. agalactiae* were isolated from the right fore, the right hind and the left forequarters. A great excess of deposit was present in the milk from the right hindquarter. Treatment commenced on December 24th and at this time clots were present in the fore milk from two of the quarters. An initial dose of 30 grammes was given and this was followed every 12 hours by 10 grammes, treatment being continued for seven days. Improvement was noticed in the milk during the course of treatment and on December 31st it was reported that only one very small and doubtful clot was found in the fore milk from the right forequarter. A bacteriological examination made on the same day, however, showed an excess of deposit in the milk from the right hindquarter and large numbers of *Str. agalactiae* in the three affected quarters.

On January 9th the owner reported that the milk was much better than it was before treatment but no marked improvement was maintained, and on January 16th some clots were present in the fore milk from the right fore- and left hindquarters.

Cow 553.—On January 1st, 1941, a bacteriological examination showed a heavy affection of *Str. agalactiae* in the right forequarter; an excess of sediment was also present in the milk from this quarter. Clots had been present in the fore milk from this quarter for some time before treatment began on January 10th and by this time the secretion from the quarter was small in quantity and straw coloured. During treatment a marked improvement occurred and on January 16th the milk from the affected quarter was normal in appearance. The milk was still

normal in appearance on February 4th, when samples were collected for bacteriological examination. The right forequarter was by this time nearly dry. The bacteriological examination showed the quarters to be still infected with *Str. agalactiae* but only a small excess of deposit was obtained on centrifuging milk from the quarter.

Cow 752.—This animal was first found to be infected with *Str. agalactiae* in both forequarters at the beginning of January, 1941. Clots were present in the fore milk from the left forequarter before treatment began on January 20th. An initial dose of 20 grammes was given, and this was followed by administering 10 grammes every 12 hours for seven days. During treatment very little, if any, improvement in the milk occurred and when a bacteriological examination was made on January 4th the left forequarter was still found infected with *Str. agalactiae*. It is unfortunate that larger doses of 4 : 4′-diaminodiphenylsulphone were not given to this animal but the supply of the compound was exhausted when treatment stopped.

None of the animals treated with 4 : 4′-diaminodiphenylsulphone showed any detectable signs of disturbance during or after treatment, and as the improvements effected on mastitis milk were similar to those produced by treating infected cattle with sulphonamide E.O.S. the owner rightly considered the former compound the better of the two, and one which he would gladly have used on all his cattle, whereas he was not keen to have more cattle treated with sulphonamide E.O.S.

Summary

Sulphonamide E.O.S. is probably as toxic for cattle as sulphanilamide. Its therapeutic value in the treatment of *Str. aglactiae* infections is limited. An improvement may be expected in the physical appearance of grossly abnormal milk during and for some time after treatment but the improvement is a temporary one. If only a temporary improvement of the milk is obtained sulphonamide E.O.S. cannot be regarded as satisfactory for the treatment of cattle on account of the diarrhoea its administration produces and the diminished milk yield that may follow, together with a general loss of condition in the animal.

4 : 4′-diaminodiphenylsulphone is of relatively low toxicity for cattle and therapeutic doses produce no symptoms of disturbance or illness. The experiments that are reported are insufficient to warrant definite conclusions regarding the value of 4 : 4′-diaminodiphenylsulphone in the treatment of mastitis but it is encouraging to find an agent which quickly improves the clinical condition of the infected udder without producing any toxic symptoms, and further experiments should be made with 4 : 4′ diaminodiphenylsulphone which appears to possess virtues equal to those of sulphanilamide but which is free from the objectionable properties of the latter.

References

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Long, P. H., and Bliss, E. A. (1939.) The Clinical and Experimental Use of Sulphanilamide, Sulfapyridine and Allied Compounds, New York.

Marshall, E. K., and Litchfield, J. T. (1938.) *Science*, **88**. 86.

Proom, H. The Lovibond comparison leaflet on the estimation of sulphanilamide and allied drugs in the blood and other body fluids.

We express our thanks to the Agricultural Research Council for a grant that covered the expenses for this work and to the Imperial Chemical Industries, Ltd., for supplies of the compounds that were tested.

CLINICAL COMMUNICATION

Radio-active Ointment Therapy in the Treatment of Warts

ALBERT EIDINOW, M.B.

Upper Wimpole St., W.

Mr. C. M——, a veterinary surgeon, *aet.* 44 years, came to see me two years ago, complaining of a large warty growth over the dorsum of the right hand. This lesion first appeared some three years ago and rapidly increased in size, until it was as large as a two-shilling piece. The wart was situated below the margin of the heads of the second and third metacarpal bones, spreading over the dorsum of the right hand. It measured roughly 3·0 cm. in diameter and was raised about 0·5 cm. above the skin surface. It was soft and showed areas of suppuration with some sero-purulent discharge. Previous treatment—when it was smaller—had failed to destroy or arrest growth of this lesion.

On May 8th, 1939, I applied a plaque of radio-active ointment (by means of technique described elsewhere). This was made by placing 2·0 c.c. of melted radio-active petroleum jelly (containing 1·0 millicurie radon per c.c.) into a cellophane envelope, 4·0 cm. × 6·0 cm. The plaque was placed over the site of the lesion, attached to the skin by adhesive strapping, and applied for 24 hours. The patient reported that there was no visible reaction following treatment and no symptoms were experienced. Suppuration subsided, the warty growth slowly contracted and became smaller and flatter, and after six to eight weeks it had healed.

I saw this patient recently—on June 3rd, 1941—nearly two years after treatment. There was a faint greyish-white area of scar tissue visible over the original site of the warty lesion ; the skin was soft—freely mobile—with good blood supply ; there was no evidence of telangiectasis or radiation scar tissue. His lesion was now quite healed—he came to see me as he now had two small warty growths at the tips of the thumb and third finger of the left hand.

ABSTRACTS

[RADIO-ACTIVE OINTMENT AS A METHOD OF SURFACE RADIUM TREATMENT. Eidinow, A. (1939.) *Proc. Roy. Soc. Med.* **32**. 553-7.]

Eidinow describes a method he has developed of using radon (a radio-active gas emitted by radium) dissolved in petroleum jelly, as a means of giving radium therapy without the risks and without certain difficulties attendant upon the use of radium itself. The chief desideratum in view was the surface treatment of skin not having a plane surface or, in other words, it was desired to apply the radio-active substance in a form allowing it to be applied evenly to irregular surfaces. In the method described radon gas supplied in capillary tubes is introduced into the desired quantity of melted petroleum jelly which is then poured into cellophane envelopes where it sets. The envelopes are used by direct application to the part, being moulded to it and covered by rubber sheeting. Radon applied in this way exerts its effects

for a few days only, owing to the natural waning of the energy inherent in it when fresh.

Radon therapy applied in this way has been successfully used against congenital naevi, telangiectasia following damage by X-rays or radium, sycosis barbae, warts and hypertrichosis.

[An interesting case record of the treatment of warts by this method is given in the Clinical Communications. Unfortunately the method must be far too expensive to find a ready use in veterinary medicine.]

J. E.

* * * * *

[THE EFFECT OF CALCIUM THERAPY UPON THE ELECTROCARDIOGRAM IN MILK FEVER. Sporri, H., and Raggenbass, A. (1940.) *Schweiz. Arch. Tierhlk.* **83**. 325-332.]

The R.T. interval of the electrocardiogram of a cow with milk fever was found to be longer than normal, indicating prolonged ventricular systole. In addition, extra-ventricular systoles occurred irregularly. The injection of calcium gluconate corrected these abnormalities but insufflation of the udder was ineffective in this respect. The same phenomena were found in guinea-pigs in which hypocalcaemia was produced experimentally by the injection of Na citrate; these were also corrected by the injection of calcium gluconate.

A. T. P.

* * * * *

[FOWL PARALYSIS: TRANSMISSION OF INFECTIVE AGENT TO YOUNG CHICKS. Glover, R. E. (1940.) **96**. 427-437.]

An infective agent was isolated from a typical case of neuro-lymphomatosis in a turkey which produced lesions in young chicks identical with those produced by agents isolated from field cases of fowl paralysis. This agent was passed through 16 generations without demonstrable modification. The author considers that probably only one agent was thus transmitted and supports the view that the initial effect of the agent is to cause acute inflammatory lesions in the young chick which are followed later by a chronic stage in which the true lymphomatous response occurs.

Attempts to produce immunity by the simultaneous injection of serum, obtained from experimentally infected chicks, and virus were negative. Formolised vaccines also proved unsuccessful.

A. T. P.

* * * * *

[OBSERVATIONS ON TORSION OF THE UTERUS IN CATTLE. Kind, G. G. (1940.) *Schweiz. Arch. Tierhlk.* **82**. 454-461.]

The author, from experience on European breeds of cattle in South Africa, says that he has never observed spiral ridges in the wall of the vagina as described by most text-books, but instead he has found two hard strands, one usually above and one below, which are the lateral ligaments of the uterus under the abnormal tension of the twist.

In treatment Kind objects to methods wherein a grip is made on the legs of the calf for the use of them as a lever; instead he relies entirely on rolling the cow by two methods, used in combination if one alone fails —(*a*) the fore legs and the hind legs of the cow (on her back) are roped and extended and she is pulled over in the same direction as the torsion, care being taken to stop the roll gradually; (*b*) in this method the roll is in the opposite direction, the hind legs being at first pressed against the body to grip the uterus and then pulled away in mid-roll, the roll being speeded up as much as possible and ending abruptly as the legs thud on the ground. This method usually succeeds.

Two cases of long standing uterine torsion plus mummified calf are also described.

J. E.

* * * * *

[SOME EFFECTS OF MENOPAUSE URINE EXTRACT ON SEXUAL ORGANS OF IMMATURE FEMALE CATS. Starkey, W. F., Leathem, J. H. (1939.) *Proc. Soc. Exp. Med. Biol.* **41**. 503-507. (7 figs., 3 refs.).]

The effects of menopause urine extract on the sexual organs of immature female cats were studied. Eight cats, averaging about nine weeks old, were treated. Five responded by stimulation of the follicles. There was marked increase in ovarian weight. Generally the right ovary responded to a greater extent than the left. The three remaining cats gave no reaction. No explanation of their defection is given.

D. D. O.

"PHENOTHIAZINE SHOULD BE USED WITH CAUTION"•

"A release from the U.S. Department of Agriculture, under date of March 18th, 1941, states that some horses and mules react unfavourably to phenothiazine. This statement is in line with the report published in the March issue of *The North American Veterinarian*, relating the loss of a number of horses following treatment with phenothiazine.

The March 18th release states that although in most instances phenothiazine treatment has appeared to be successful, 'some reports of deaths or unfavourable reactions' have reached the U.S. Bureau of Animal Industry. Whether these resulted from the use of the drug, or from some condition that existed in the animals at the time of treatment, is not known.

There never has been a drug that was so widely and actively exploited among livestock owners as phenothiazine. About everything that could be said in favour of phenothiazine appeared in print. It was efficient, harmless and cheap. What more could be asked of a drug? It fulfilled every requirement for exploitation. Many parasites thought that the game was up.

Although a little bit late, it is somewhat comforting to read the warning contained in the Washington release of March 18th:—

> Treatment of any kind for removing intestinal parasites should be undertaken only when an examination of the droppings with microscope, by a qualified veterinarian, shows it is warranted. In some cases, animals apparently in good condition have suffered from use of the drug.
>
> Wholesale treatment should be avoided. . . .
>
> In all instances the diagnosis of parasitism should be made and the treatment given by a qualified veterinarian.

Attention is invited to the article from the Oregon State College, published in this issue, reporting some rather disappointing results of the treatment of sheep with phenothiazine.

The story of phenothiazine follows a well-known American formula. We have passed through the period of excitation and are now going through the period of more sober rationalism. Some time later on, we hope that someone will evaluate phenothiazine as an anthelmintic with a reasonable degree of accuracy."

• Reproduced from *The North American Veterinarian*, Vol. 22, No. 5, May, 1941, p. 262.

ROYAL COLLEGE OF VETERINARY SURGEONS

Membership Examinations (July, 1941)

LIST OF SUCCESSFUL CANDIDATES

(*Continued from page* 424.)

Dublin:

FIRST YEAR:

Burke, W. L. (B)
•Bryson, H.
Byrne, P. J.
Coe, T.
Crooks, D. (B)
•Cronin, M. T. I.
Canavan, R. J.
Corcoran, C. J. (B)
Clyde, D. H. (B)
Donnelly, J.
Erskine, R. G. (B)
Eakins, F. S.
†Farrelly, B. T.
Greenwood, J. J. (B)
†Hamilton, A. H. A.
Harbison, J. T. (B)
Hatton, R. D.
Higgins, P. K. (C)
Hill, H. J. (B)
•Jordan, H.
Kealy, B.
Kelly, W. H. B. (B)
Lacey, de T. (B)
Loughlin, E. (C)
Lunny, W. J. (C)
•McCrea, G. H.
McFerran, A. M. (C)
McGroarty, D.
McGuinness, T. P. H.
McNeill, J.
Mockler, P.
Moore, G.
Murphy, Michael (C)
O'Connor, Joseph
O'Shaughnessy, T. (B)
Powell, W. V.
Richardson, J. P. (B)
Ross, J. K. (B)
Sherriff, R. B. (B)
•Simpson, T. T.
Tobin, W.

†Denotes first class honours.
•Denotes second class honours.
(C) Denotes credit in Chemistry.
(B) Denotes credit in Biology.

SECOND YEAR:

Barron, J. M. (P)
Black, R. A. (H)
Boyd, N. C. (P)
Casey, P. M. (P)
Clarke, A. R. L.
Cooney, J.
•Curtis, R. G.
•Dancey, G. F.
•Earnshaw, R. E.
Finlay, J. T. T. (P)
Fitzpatrick, D. (P)
•Gilmore, R. A.
Gleeson, E. (P)
Harris, K. A.
Hunt, T. G. (H)
Kay, E. D.
•Kelly, D. L.
King-Hall, R. (P)
McCarroll, P. J.
McKnight, R. W.
McNally, G. K.
•Marshall, J. V. O.
Moloney, E.
•Mullin, W. J.
O'Farrell, J. D.
McBride, P. S.
McGrenra, D. P.
Mone, P. B.
O'Brien, W. B.
•Sweeney, P. A.
Timmins, E. H.
Wall, B. (P)
Wolfe, F. E.
Yourell, Miss J.

•Denotes second class honours.
(P) Denotes credit in Physiology, etc.
(H) Denotes credit in Histology, etc.

THIRD YEAR:

Aitken, J.
Burke, S. E.
Carmichael, R. (P) (A)
Coyle, M. J.
Dalzell, K.
Dolan, M. M. (P)
Eivers, B. W. (P)
Fitzgerald, Miss P. (A)
Fitzgibbon, J. P.
Foley, J.
Freeman, W. J.
Geaney, D.
Halpin, F. B. (A)
Hodgins, R. D.
Huey, J. (H)
Jackson, T. W.
†Kelly, W. R.
•Lee, R. P.
Leonard, T. B.
McAtee, P. G. (P)
McCarroll, J. J.
McFarland, M. J. (A)
•McGarry, J. J.
O'Connor, J. G.
O'Neill, W. D.
Roe, M. C. (A)
Steele, H. J. (P)
Tufts, F. A.
Scannell, P.
Shinnors, G. A.
Smyth, A.

†Denotes first class honours.
•Denotes second class honours.
(P) Denotes credit in Pharmacology.
(A) Denotes credit in Anatomy.
(H) Denotes credit in Hygiene.

FOURTH YEAR:

Allison, P. T. M.
Blake, P. A.
•Burgess, D.
Condron, C. G.
Duigan, T. J.
Farrell, H. F. (Path)
Forgie, S. A.
Good, N. S.
Johnston, J.
McClay, M. S.
•McErleam, B. A.
Magee, B. L.
Mahony, I. J. (Path)
Morgan, F. J.
Mullan, F. (Path)
•Orr, F. H.
Parkhill, J. P. (Paras)
Ray, N.
•Scally, W. C. P.
Sheehy, P. J.
Stewart, J. E.

•Denotes second class honours.
(Path) Denotes credit in Pathology.
(Paras) Denotes credit in Parasitology.

FINAL EXAMINATION:

Audebert, M. B. (•)
Bowen, L. T.
Byrne, D. G.
Carlisle, J.
Davison, W. F.
Dodd, A. M.
Donnelly, A. D.
Fletcher, W. E. (S)
Gallagher, M. Anthony (S)
Griffiths, O. V.
Hutch, L. (S)
Kavanagh, S.
Kinsella, L. K.
Kinney, J.
Lynch, T. J.
Meegan, P. A.
O'Kennedy, J. K.
Parkill, Miss E.
Power, W. P.
Quinn, B. J.
Thompson, T. W. (S)
Whitty, B. T. (S)
Yasin, S. A.

(S) Denotes credit in Surgery.
(•) Denotes By-law 95 candidate.

Glasgow

SECOND YEAR:

Bannatyne, C. C.
Boyle, J. G. S.
Corbett, Miss B.
•Denholm, T. C.
Donald, Miss Nancy
•Foster, A. H.
Gillies, R. J. M.
Gregg, J. R.
•Hartman-Smith, C. A.
•Hastie, P. S.
McIntee, D. P. (H)
Maguire, R. D. (H)
Markson, L. M. (H)
Martindale, P. D.
Mitchell, David
•Parker, Joseph
Roberts, R. M.
Spirman, Otto
Usher, F. J.

•Denotes second class honours.
(H) Denotes credit in Histology, etc.

FOURTH YEAR:

Barratt, A. J.
Bayliss, J. B. (Paras)
Brown, J. (Glasgow)
Bryson, I. C.
Coleman, J. G.
Douglas, Robert
Flynn, A. S.
Hill, David
Holt, A. F.
Johnston, Adam
McElhone, J. S.
Mackay, J. R.
Mathieson, N. H.
Miller, Andrew
Moir, R. S.
Paterson, R. A.
Pearson, J. K. L.
Quigley, P. J.
Samuel, Miss M. I.
Scott, K. E.
Skillen, W. W.
Thain, R. I.
Watson, Miller
Wilson, W. R.
Wilson, Robert

(Paras) Denotes credit in Parasitology.

Final Examination:

Anderson, A. C.	Harris, G. W.
Auld, Robert	Haxton, David
Black, T. M.	Paterson, A. B.
Black, W. W.	Rankin, J. D.
Brown, J. (Airdrie)	Semple, William
Cairns, J. T.	Shaw, D. B.
Caldwell, W. D.	Swanney, J. M.
Cassells, Joseph	Thompson, J. J.
Dunlop, F.	Twiss, A. F.
Ferguson, C. M.	

Liverpool

Second Year:

Adams, A. D.	Humphreys, J. R.
Done, J. T. (P)	Kay, R. S.
Fox, H. J. (P)	*Littlejohn, Miss A. I.
Hall, C. A.	*Maddocks, J. T.
Hawkins, R. H.	Pinsent, P. J. N. (P)
Hewitt, S. L.	Robinson, Peter
Hughes, A. L.	

*Denotes second class honours.
(P) Denotes credit in Physiology, etc.

Third Year:

Chapman, F. A. (A)	Roberts, H. R.
Cohen, C. A. (P)	Saunders, C. N. (P) (A)
Edwards, A. M.	Singleton, A. G.
Ford, E. J. H. (A)	Towers, K. G. (P) (A)
Jennings, A. R. (A) (H)	Wood, J. C. (A) (H)
Loosmore, R. M. (A) (H)	

(P) Denotes credit in Pharmacology, etc.
(A) Denotes credit in Anatomy.
(H) Denotes credit in Hygiene.

Fourth Year:

Bolton, J. F.	Jubb, Miss S. C.
Boundy, Terry	Kerr, P. A.
Campbell, J. A.	MacLennan, I. S.
Carlyle, Arnold (Path)	Pearson, R. W. H.
Jones, E. B.	Richards, R. A. (Path)
Jones, James	Unsworth, Kenneth
Jones, W. M.	Wilson, Miss M. E. M.

(Path) Denotes credit in Pathology.

Final Examination:

Bee, B. R.	Hopkins, C. D.
Clay, H. A.	Jones, D. K.
Davies, D. B.	Willis, G. A.
Donnelly, J. F.	Wilson, A. A.

(To be concluded.)

Erratum.—In Edinburgh list, published last week, at top of col. 2, p. 424, *for* "Second year" *read* "Third year."

Weekly Wisdom

"Personal opinions are of small importance compared with hard facts. Their value is solely the combination of two factors—accuracy of information and sound judgment. Acknowledged ability in a man in one capacity may lead people to value his personal opinion on other subjects, because from his ability he is credited with sound judgment, whereas the information he may possess on which to base an opinion may be far from accurate or complete. Conversely, a person possessing unique knowledge of a subject, usually termed an expert, may be lacking of that extraordinary gift of judgment which enables him to assess the value and make allowance."—From "Times" letter on armaments.

* * * * *

A further cheque for £25,000 has been presented to the Red Cross and St. John War Organisation by the Red Cross Agriculture Fund.

IN PARLIAMENT

Pharmacy and Medicines Bill

The Committee stage of the above Bill was concluded in the House of Commons on July 16th, when a general discussion took place on Clause 6 on a number of amendments designed to secure that the ingredients of medicines the composition of which are required by the Bill to be described on the wrapper or bottle should be so described in language which the general public could readily understand.

Mr. J. Griffiths moved an amendment providing that the description of the ingredients should be in English.

Mr. E. Brown, Minister of Health, expressed sympathy with the hon. Member's object, but pointed out the technical difficulties in the way of describing medicines in simple English terms. Moreover some names, though they might be English, might not be easily recognisable. He suggested that an amendment which he had on the paper deleting the word "composition" and inserting the words "accepted scientific name or other name descriptive of the true nature," would avoid the technical difficulties to which he had referred and at the same time meet the wishes of the Committee in this respect. If hon. Members would withdraw their amendments at this stage and accept his he would undertake to consider the question further before the Report stage and see whether anything further could be done to meet the desires of the Committee.

The amendment was, by leave, withdrawn and Mr. Brown's amendment was agreed to.

Sir T. Moore moved an amendment to Clause 6 to safeguard the position of herbalists.

Miss Horsbrugh, Parliamentary Secretary, Ministry of Health, said the Committee had agreed there should be the clearest possible disclosure of the contents of a remedy, and it would be unfair to exclude one class from the necessity for disclosure.

The amendment was negatived.

Mr. E. Brown accepted an amendment, moved by Captain Elliston, postponing from January 1st to July 1st next the coming into operation of Clause 6, which provides for the disclosure of composition of medicines. The amendment was agreed to.

* * * * *

Among the questions and answers recorded in the House of Commons recently were the following:—

Colonial Development Grants

Captain Dugdale asked the Under-Secretary of State for the Colonies why it is that only £400,000, out of a total of £5,000,000, allocated for this purpose under the Colonial Development Act has, in fact, been voted for schemes to be carried out during the year 1941-42?

Mr. George Hall: At the time when this estimate was framed, it was expected that, owing to war conditions, it would not be possible to spend more than the amount mentioned by my hon. and gallant Friend on new schemes under the Colonial Development and Welfare Act during the current financial year. But it was always the intention that if we found ourselves able, as indeed I now hope will be the case, to make grants involving expenditure during the year in excess of that amount, Parliament would be asked to make the necessary financial provision on a Supplementary Estimate.

* * * * *

Colonial Post-war Reconstruction (Hailey Committee

Mr. Creech Jones asked the Under-Secretary of State for the Colonies what is the composition of the body set up in the Colonial Office under the chairmanship of Lord Hailey; what are its terms of reference; what outside bodies and groups it will work with or consult; and whether such an organisation will be asked for its recommendations on Colonial policy and post-war relations, development and future changes?

Mr. George Hall: The body to which this Question refers is a small committee composed, apart from the Chairman, of senior members of the Colonial Office staff. Its purpose is to prepare a statement of the political, administrative, economic and social questions which are likely to come up for consideration in relation to the Colonies at the end of the war; and to assemble, so far as is practicable, the facts and other material which will be required for the consideration of these questions. The committee will seek the aid of such persons and organisations as may be in a position to supply information of the kind that is required. This committee, as has been stated in another place, is primarily a preliminary fact-finding body; and it will be a matter for consideration at a later date whether it should be invited to submit recommendations on policy, post-war relations, development and future changes.

Mr. Creech Jones: Will there be any connection between this Committee and the research organisation Nuffield College? Also, in the shaping of policy, will there be the fullest consultation with all other types of outside organisations?

Mr. Hall: That is a matter which will be considered by Lord Hailey and his Committee. The Committee has only just been set up, and it will take into consideration all the Questions that the hon. Member has put.

. . . . .

Food Supplies: Synthetic Vitamins

Mr. Mander asked the Parliamentary Secretary to the Ministry of Food into what form of food the minimum daily requirements of the most important vitamins and minerals are being introduced; whether he is aware that the United States of America are anxious to send us synthetic vitamins occupying negligible shipping space; and whether advantage will be taken of this?

The Parliamentary Secretary to the Ministry of Food (Major Lloyd George): Steps are being taken to obtain from the United States of America such quantities of vitamin as my noble Friend is advised are desirable to supplement the amounts available in the form of natural foods. Medical and scientific advisers consider that the only mineral deficiency which is to be feared under war-time conditions is in respect to calcium. Recommendations for dealing with this possible deficiency are now under consideration.

. . . . .

Feeding-stuffs (Milk Production)

Mr. Leach asked the Minister of Agricuture whether he is aware that farmers in urban areas, with little pasture for feeding purposes, are suffering an acute shortage of cattle food with damaging consequences to the production of milk; and can he release for their benefit further supplies of cake, meal or other foods.

Mr. Hudson: The main problem is to safeguard the milk supply in winter. Owing to the short supplies of imported feeding-stuffs and the need to establish reserves for winter use it is essential that dairy cows should be kept to the maximum extent on pasture during the summer. Farmers who keep cows intensively and who normally buy large quantities of feeding-stuffs in relation to their milk output were warned in April that they should make arrangements to adjust themselves to the conditions of shortage of concentrates that would obtain during the summer months. A supply of concentrated feeding-stuffs has been placed at the disposal of each county war agricultural executive committee for issue to dairy farmers whose pasture deteriorates quickly in quality and quantity and a number of other measures have been adopted during the summer to counteract deficiencies in pastures. I regret that in view of the present supply position it is not possible to make available any further quantities of concentrates at the present time.

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Scientific Advisory Committee

Captain Plugge asked the Lord President of the Council what liaison has been established between the Scientific Advisory Committee and the various scientific and technical institutions in this country?

The Lord President of the Council (Sir John Anderson): Liaison with the numerous scientific and technical institutions maintained or assisted by the Government is established through the Secretaries of the Department of Scientific and Industrial Research, the Medical Research Council and the Agricultural Research Council, who are members of the Committee, as well as through the Directors of Scientific Research at the Admiralty, Ministry of Supply, Ministry of Aircraft Production and Ministry of Home Security. Liaison with other scientific institutions is maintained, as most convenient, either through the official channels I have just mentioned or through the President and Joint Secretaries of the Royal Society, who are also members of the Committee.

Mr. Hannah asked the Lord President of the Council what scientific problems have so far been referred to the Scientific Advisory Committee?

Sir J. Anderson: It would not be in the public interest to give particulars of the scientific problems dealt with by this Committee, whose proceedings are of a highly confidential nature.

NOTES AND NEWS

The Editor will be glad to receive items of professional interest for inclusion in these columns.

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PERSONAL

Colonel R. J. Stordy's Illness.—Following upon our recent notification, which was received with widespread regret, of the illness of Colonel R. J. Stordy, Chief Executive Officer of the National A.R.P. for Animals Committee, we are glad to be able to report that an operation for relief of stoppage of the bile duct has been performed successfully. Although the Colonel is still extremely ill, it is believed that he is making slow but sure progress toward recovery.

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Marriage.—Weatherhead—Palmer.—On July 17th, at Trinity Church, Brompton, Gerald Candy Weatherhead, B.A., M.R.C.V.S., to Eleanor Victoria (Bunty) Palmer.

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COMPOSITION OF THE AGRICULTURAL IMPROVEMENT COUNCIL FOR SCOTLAND

Sir Arthur Olver's Protest

"The composition of the recently announced Agricultural Improvement Council for Scotland, 'to devise methods for seeing that promising results of research are applied as rapidly as possible to the problems of agriculture and are incorporated in ordinary farming practice; and to advise from time to time concerning agricultural problems which appear to require scientific investigation,' must, I feel sure, have caused as much astonishment to Scottish farmers as it has to the veterinary profession," writes Sir Arthur Olver, Principal of the Royal (Dick) Veterinary College, in a letter which has been accorded wide publicity by the Scottish Press. Sir Arthur proceeds: "The purpose for which the Council has been formed is essentially the practical application of the results of research to Scottish agriculture, and its composition is as follows: Four Civil Servants, members of the Department of Agriculture for Scotland; six representatives of Scottish Agricultural Colleges; two medical men, and a representative of Scottish farm workers.

"Whether Scottish breeders will feel that they are suitably represented, I do not know, but it is surely astonishing that there is not one veterinarian or anyone on the staff of any of the Scottish research institutions

which constantly deal with matters of the greatest practical importance to stockowners—such as the Animal Diseases Research Association, the Institute of Animal Genetics, the Rowett or Hannah Institutes—or of the Scottish Veterinary Colleges.

"Neither are there any members of the official veterinary services for disease control and public health work, nor any of the veterinary practitioners on whom the success of livestock production so much depends.

"It may be assumed that the two medical men have been appointed because of their connection with the Agricultural Research Council or the Animal Diseases Research Association, for neither can claim the intimate knowledge of livestock and Scottish farming conditions which ought to be an essential qualification for a seat on this important Council. In any case, with all due respect to the personal ability of these two members, it cannot be admitted that medical men satisfactorily represent the veterinary profession in regard to the wide range of practical problems which this Council must deal with, if it is to produce any material improvement in war-time production or satisfactory reconstruction of Scottish farming after the war.

"Nor can it be admitted that suitable representatives are not to be found in Scotland, able to deal satisfactorily with veterinary research and the control of disease among livestock, with their scientific feeding and management, or with the sanitary control of the production, handling and disposal of animal products, such as milk and meat.

"In the corresponding Council in England two veterinarians are included, which is scant representation enough, and in view of the even greater preponderance of livestock in Scottish farming, I feel it my duty to draw attention to the paucity of the representation of livestock interests on this Scottish Council.

"It seems to have been overlooked that 80 per cent. of the returns from Scottish agriculture are derived from livestock, and that it is reliably estimated that the loss sustained by the farming industry of Great Britain from disease among livestock amounts to at least £20 millions a year.

"In the course of 50 years' experience of the breeding and management of pedigree stock and of veterinary and animal husbandry work—including 40 years of public service in a variety of appointments—I have worked for years in or in close association with comprehensive animal husbandry organisations, under veterinary control, which deal with all aspects of animal industry and are well known to have produced results of the greatest economic and sanitary importance to the countries concerned; for example, the Union of South Africa and the U.S.A.

"Experience of similarly organised and controlled animal husbandry work in other countries, including work under my own direction, has, in fact, shown very strikingly that, given the far wider powers and facilities which are accorded to veterinarians in all the most progressive livestock countries of the world, veterinary science could be of the greatest practical value to the livestock industries of Great Britain.

"In any case, in view of the vital importance of maintaining the yield of animal products during the war, of conserving our herds and flocks for after-war reconstruction, and because of the increased danger, under war-time conditions, of infection from milk- and meat-borne diseases such as tuberculosis and trichinosis—I submit, with all respect, that veterinarians and other suitably trained scientific workers, who constantly deal with livestock problems in their daily work, ought to be more suitably and adequately represented on this Council."

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SICK DOGS MUST NOT BE FED FOOD FIT FOR HUMAN CONSUMPTION

We publish the text of correspondence which has passed between the Association and the Ministry of Food on a subject of considerable importance to practising veterinarians.

On June 24th, Mr. F. Knight, the Secretary, N.V.M.A., addressed the following letter to the Secretary of the Ministry of Food:—

"It was stated in *Our Dogs* of May 30th that the Editor of that publication had asked the Ministry of Food if a person who gave any food fit for human consumption to a sick dog would be guilty of an offence against the regulations, and that in a letter signed by R. Wentworth the Ministry had given the following reply:—

> "In reply to your letter of April 23rd regarding the use of food suitable for human consumption as food for sick dogs, I am directed to inform you that such use would constitute an offence against the Waste of Food Order, 1940 (Statutory Rule and Order 1424/1940), and cannot be permitted.
>
> "If advice to use such food for the purpose described were given, both the person following the advice and the one giving it would be liable to heavy penalties."

"As this ruling affects members of the veterinary profession I am instructed to ask for guidance from the Ministry as to the position of the veterinary surgeon giving advice to his client, in order that a statement on the point may be published in the Association's journal."

On July 17th Mr. R. Wentworth replied as follows, on behalf of the Ministry of Food:—

"With reference to your letter of June 24th, in which you quote from my letter of April 23rd last, addressed to the Editor of *Our Dogs*, regarding the use of human food as food for sick dogs, I am directed to inform you that the second paragraph quoted by you must be regarded as applying equally to cases where veterinary surgeons advise the use of such food for the purposes mentioned."

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NEW WAR DAMAGE BILL

Extension of Risk Period

On July 16th the Chancellor of the Exchequer introduced in the House of Commons a Bill by which payments under Part 1 of the War Damage Act for damage to houses and other buildings by enemy action will be extended for a second "risk period" of 12 months ending on August 31st, 1942.

Payments under the original Act may be made only in respect of a "risk period" extending from the beginning of the war to August 31st this year. The new Bill—entitled the War Damage (Extension of Risk Period) Bill—will ensure that compensation payments are continued for another year, pending more comprehensive legislation on war damage later.

The new Bill will make no change in the amount of contributions payable under the present Act. Those payable for the second "risk period" provided by the new Bill will be determined by Parliament when the further legislation is considered. This means that until another Bill is passed later in the year the only war damage contribution to be collected will be the 2s. in the £ on the net Schedule A value (or net rateable value) of property which is payable each year for five years from July 1st, 1941, to cover compensation payments during the first "risk period."

In addition to the rate of contribution for the second "risk period," legislation to be introduced later will include such amendments of the War Damage Act as may prove necessary from the experience of its working.

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FOOT-AND-MOUTH DISEASE: A LESSON FROM EIRE

For six months previous to the recent despatch of cattle and sheep from Dublin to a cross-Channel port, the export of cattle from Eire had been forbidden owing to the worst epidemic of foot-and-mouth disease in the country's history. It led to the slaughter of nearly 20,000 cattle, together with a great many sheep and pigs; its cost to the Free State Government is estimated at £233,000.

The primary infection is believed to have reached Donegal from Northern Ireland, but the spread of the disease throughout Eire, says the *Irish Times*, was "due almost entirely to the folly and carelessness of the people themselves. If the Department's orders had been obeyed conscientiously from the start the original outbreak might have been isolated; but, as happens so often in this country, numbers of people, including the farmers, who stood to lose most heavily, simply ignored the precautions which ought to have been taken."

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BREWERS' GRAINS AN OFF-RATION FEEDING-STUFF

Brewers' wet grains are "off the ration" and can be bought without coupons. "It is a chance for dairy farmers to build up a valuable reserve of feeding-stuff for winter use," states the Ministry of Agriculture in a recent announcement, "but the grains must be stored under air-tight conditions or they will turn sour and mouldy. Pits are the best places in which to store them, and if the pits can be lined with brick or concrete, so much the better. The proceeding is very similar to silage making and the Ministry has issued a new war-time leaflet (No. 67. *Brewers' Wet Grains for the Winter*) with some useful guidance about storage and some remarks upon the quantities to feed. It is free on application to the Ministry at Hotel Lindum, St. Anne's-on-Sea, Lancashire."

CORRESPONDENCE

Letters to the Editor should reach the Office not later than by the first post on Tuesday morning for insertion in following Saturday's issue.

The views expressed in letters addressed to the Editor represent the personal view of the writer only and must not be taken as expressing the opinion or having received the approval of the N.V.M.A.

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"A PRACTITIONER'S COMPLAINT"

To the Editor of the Veterinary Record

Sir,—While I cannot help feeling a little envious towards Mr. Muir's good fortune in practice, his letter in your current issue is so much at variance with conditions as I have found them that I feel prompted to add my contribution to the subject under review.

In contrast to Mr. Muir, I believe I am correct in stating that a large number of practitioners in agricultural districts find a large proportion of their work, to say the least, much less remunerative than it should be in view of the labours involved.

The primary reason for this state of affairs, as I see it, is the combination, at the present time, of the following factors: the low economic value of so many of the cases we are called upon to treat; the restricted financial status of many of the smaller clients together with the heavy mortality and unsatisfactory outcome of so many of the cases treated; the fact that we live amongst people's bad luck and misfortunes.

Even with low values, if it were possible to be assured of the final outcome before attempting treatment, or if one could rely on a consistent series of successes, conditions would be very different. Treatment of farm animals is, however, practically devoid of sentiment and based on hard economic facts. For this reason unless the practitioner is able to produce results in long-drawn-out cases it would often be ridiculous to send in charges commensurate with the labour involved.

Most veterinary surgeons of experience seem to develop a sense of proportion and tolerance and a faculty for seeing the other man's point of view, and have a fair idea of the fee they are able to charge or in certain cases of hardship care to charge.

I believe that those who have never engaged in practice are not aware of the number of unsatisfactory cases which occur.

I think it should be stated that there is no dearth of veterinary surgeons who, to use Mr. Muir's words, "have the goodwill of the agricultural community, and are giving efficient service at a moderate cost." I would go even further than Mr. Muir and assert that there are many practitioners of my acquaintance who have far more interest in the welfare of their cases than in the emoluments received.

I fail to see, therefore, why it is a weak-kneed policy for the practitioner to be anxious to retain a form of service with regular rates and assured fees, which is a very definite offset to the less lucrative side of practice.

I feel, however, that Mr. Muir's letter raises a far wider issue: whether the time is not opportune for the N.V.M.A. to explore the possibilities of a panel system to include the whole of agricultural practice or the extension of the scheme already under review.

Yours faithfully,
O. V. Gunning.

Acle,
Norwich.
July 20th, 1941.

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To the Editor of the Veterinary Record

Sir,—I am very grateful to Mr. Muir for his sympathy, but I regret that he apparently only perused my letter, without appreciating and correctly interpreting my remarks.

My reference to the disagreeable side of practice is chiefly, as stated, relative to the introduction of further legislation, having in mind the suggested scheme for the eradication of mastitis, sterility, abortion, etc., which may be followed by even further schemes, when, I fear, the Ministry might consider the necessity of further supplementing their permanent staff, to the disadvantage of the practitioner, who has always been the mainstay of the profession. With the advent of State Veterinary Service in the offing our position must be made secure.

Where Mr. Muir finds the suggestion of subsidy I cannot imagine. I certainly make no appeal to charity, but I do think that those in distressed areas might be given a little consideration. I state a case calling attention to a situation which appears to be developing, with a view to getting it corrected before it is too late, and demand only those rights to which surely we are entitled.

I make not the least complaint against the farmer, recognising in him a friendly associate, and reiterate that it would be to our mutual advantage if a reasonably generous Government Department were responsible for our fees.

I am glad to hear that, based on such a lengthy experience of this agricultural neighbourhood, Mr. Muir's accounts are so efficiently managed and that he attaches so little importance to the Ministry of Agriculture appointments. I suggest that if he finds so much of their work so distasteful he should forgo any advantages that it has to offer, to the benefit of a practitioner who appreciates its attractions.

The definition of "a proverb" can be found in the English Dictionary.

Faithfully yours,
W. Shipley.

Southtown,
Great Yarmouth.
July 21st, 1941.

Scotsmen consider that the general quality of their beef cattle is so high that there need be no special steps to cull unthrifty animals. This claim is made by the Scottish Department of Agriculture in a note of advice to farmers.